REMARKS

With the instant Amendment, Claims 68-71 are canceled without prejudice, and Claims 78-82 are amended. After entry of the instant Amendment, Claims 1-8, 11, 13-15, 21-23, 26-32, 35, 36, 40, 41, 44, 50-52, 60, 64, 65, 72-83 are pending and under consideration. While Claims 66 and 67 were listed as pending in the Office Action mailed November 20, 2002, Applicants respectfully note that both Claims 66 and 67 were canceled in their Amendment and Response mailed August 26, 2002. Applicants note with appreciation the PTO's acknowledgment that Claims 1-8,11, 13-15, 21-23, 26-32, 36, 40, 41, 44, 50-52, 60, 64, 65, and 72-77 recite allowable subject matter.

I. THE AMENDMENT OF THE CLAIMS

Claims 78-82 have been amended to update their dependencies to reflect the cancelation of Claims 68-71. The amendments of Claims 78-82 are fully supported by the specification and claims as originally filed and do not introduce new matter. Accordingly, entry into the instant Application is respectfully requested.

II. THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 35 and 79 stand rejected under 35 U.S.C. § 112, second paragraph, allegedly for being vague and indefinite because it is unclear how any kind of three-dimensional porous substrate has a void volume. The PTO states that "it is known that the void volume is defined as the volume of mobile phase in a column having a resin comprising beads. However, independent claims 1, 60, and 68-77 do not limit claimed flow-through device as a column having a resin comprising beads."

Although the definition of void volume supplied by the PTO is used in the field of column chromatography, this definition is too narrow, since void volume is broadly viewed as a property of any porous medium such as rock, soil, ceramics, zeolites, etc., through which liquid or gas can flow. For example, void volume is defined as the "[t]otal empty spaces in a compacted mix" in the *BNI Building News Construction Dictionary* (BNI Publications, Los Angeles, 1999), p. 571. Indeed, the concept of void volume is central to that of porosity, which according to the *Materials Handbook*, 13th ed. (McGraw-Hill, Inc., New York, 1991), p. 961, is defined as "[t]he ratio of the *volume of the interstices* of a material to the volume of

its mass" (emphasis added). It is readily apparent that void volume, as used by applicants, for example, in the specification on page 31, lines 16-18, and in Claims 35 and 79, is synonymous with the volume of the interstices. Thus, one recognizes that any three dimensional porous substrate may have a void volume, including a flow-through device as recited in independent claims 1 and 60.

Since a person of skill in the art would easily understand what is meant by void volume, Applicants respectfully request the withdrawal of the rejections of Claims 35 and 79 under 35 U.S.C. § 112, second paragraph.

III. THE REJECTIONS UNDER 35 U.S.C. § 102

Claims 68, 78 and 80-82 stand rejected under 35 U.S.C. § 102(b) allegedly as being anticipated by Van Ness *et al.* (U.S. Patent No. 5,667,976). Without agreeing with the propriety of the rejection, Applicants submit that the cancelation of Claim 68 renders the rejection of Claim 68 under 35 U.S.C. § 102(b) moot. Therefore, Applicants respectfully request the withdrawal of the rejection of Claim 68 under 35 U.S.C. § 102(b).

Applicants submit that the rejections of Claims 78 and 80-82 are obviated as a result of the amendments to Claims 78 and 80-82. Claims 78 and 80-82 have been amended to no longer depend from Claim 68 and, as amended, Claims 78 and 80-82 depend solely from allowable Claims 72-77. Accordingly, Applicants respectfully request the withdrawal of the rejections of Claims 78 and 80-82 under 35 U.S.C. § 102(b).

IV. THE REJECTIONS UNDER 35 U.S.C. § 103

A. Rejections of Claim 69

Claim 69 stands rejected under 35 U.S.C. § 103(a) allegedly as being obvious over Van Ness *et al.* (U.S. Patent No. 5,667,976) in view of Beattie (U.S. Patent No. 5,843,767). In addition, Claim 69 stands rejected under 35 U.S.C. § 103(a) allegedly as being obvious over Kamb *et al.* (U.S. Patent No. 6,060,240). Without agreeing with the propriety of these rejections, Applicants submit that the cancelation of Claim 69 renders any rejection of Claim 69 under 35 U.S.C. § 103 moot. Accordingly, Applicants respectfully request the withdrawal of the rejections of Claim 69 under 35 U.S.C. § 103(a).

B. Rejections of Claims 70 and 71

Claims 70 and 71 stand rejected under 35 U.S.C. § 103(a) allegedly as being obvious over Van Ness *et al.* (U.S. Patent No. 5,667,976) in view of Chamberland (Canadian Patent 1,110,511). Without agreeing with the propriety of these rejections, Applicants submit that the cancelation of Claims 70 and 71 renders any rejection of these claims under 35 U.S.C. § 103 moot. Accordingly, Applicants respectfully request that the rejection of Claims 70 and 71 be withdrawn.

C. Rejection of Claim 83

Claim 83 stands rejected under 35 U.S.C. § 103(a) allegedly as being obvious over Van Ness *et al.* (U.S. Patent No. 5,667,976) in view of MacConnell (U.S. Patent 4,787,963). Claim 83 has been amended to depend from Claims 72-77, which as noted by the PTO, recite allowable subject matter. *See* Office Action mailed November 20, 2002, page 11, item 12. Applicants submit that the rejection of Claim 83 is obviated as a result of the amendment to Claim 83. Therefore, Applicants respectfully request that the rejection of Claim 83 be withdrawn.

CONCLUSION

Applicants submit that Claims 1-8, 11, 13-15, 21-23, 26-32, 35, 36, 40, 41, 44, 50-52, 60, 64, 65 and 72-83 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 1-8, 11, 13-15, 21-23, 26-32, 35, 36, 40, 41, 44, 50-52, 60, 64, 65 and 72-83 to issuance is therefore kindly solicited.

No fees in addition to the extension fee are believed due in connection with this response. However, the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds LLP U.S. Deposit Account No. 16-1150.

Respectfully submitted,

Date 3/20/05

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Enclosure (Exhibits A and B)

EXHIBIT A

MARKED UP VERSION OF AMENDED CLAIMS

78. (Amended) The flow-through device of Claim [68, 69, 70, 71,] 72, 73, 74, 75, 76 or 77 in which said capture polynucleotide is covalently attached to the porous substrate.

79. (Amended) The flow-through device of Claim [68, 69, 70, 71,] 72, 73, 74, 75, 76 or 77 in which said porous substrate has a void volume in the range of about 1 $\mu l/cm^2$ to about 100 $\mu l/cm^2$.

80. (Amended) The flow-through device of Claim [68, 69, 70, 71,] 72, 73, 74, 75, 76 or 77 in which the capture polynucleotide is covalently immobilized on the porous substrate via its 5'- or 3'- terminal residue.

81. (Amended) The flow-through device according to Claim [68, 69, 70, 71,] 72, 73, 74, 75, 76 or 77 further comprising a housing in which the three-dimensional porous substrate is disposed.

82. (Amended) A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim [68, 69, 70, 71,] 72, 73, 74, 75, 76 or 77 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

EXHIBIT B

PENDING CLAIMS AFTER ENTRY OF INSTANT AMENDMENT

1. (Three times amended) A flow-through device for capturing a target nucleic acid comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having immobilized thereon about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid, and wherein said porous substrate is about 1 mm to 20 mm thick.

2. (Thrice Amended) The flow-through device of Claim 60 in which said porous substrate is about 1 mm to 20 mm thick.

3. (Thrice Amended) The flow-through device of Claim 1 in which said porous substrate has an average pore size of about 1 μm to about 250 μm.

4. (Thrice Amended) The flow-through device of Claim 60 in which said porous substrate has immobilized thereon about 2×10^{-19} to 2×10^{-15} nmol/nm^2 of said capture polynucleotide.

5. (Twice Amended) The flow-through device of Claim 1 or 60 in which said capture polynucleotide is covalently attached to the porous substrate.

6. (Twice Amended) The flow-through device of Claim 1 or 60 in which said capture polynucleotide is covalently attached to the porous substrate *via* a phosphodiester, phosphorothioate or phosphoramidate linkage.

7. (Twice Amended) The flow-through device of Claim 1 or 60 in which said capture polynucleotide is covalently attached to the porous substrate *via* a carboxyamide linkage.

8. (Thrice Amended) The flow-through device of Claim 1 or 60 in which said capture polynucleotide is covalently attached to the porous substrate *via* a linker.

11. (Thrice Amended) The flow-through device of Claim 1 or 60 in which said porous substrate has a void volume in the range of about 1 μl/cm^2 to about 100 μl/cm^2.

13. (Thrice Amended) The flow-through device of Claim 1 in which the porous substrate has a porosity in the range of about 25 to 80%.

14. (Thrice Amended) The flow-through device of Claim 1 or 60 in which the capture polynucleotide is covalently immobilized on the porous substrate via its 5'- or 3'-terminal residue.

15. The flow-through device of Claim 14 further including a linker disposed between the porous substrate and the capture polynucleotide.

21. (Thrice Amended) The flow-through device according to Claim 1 or 60 further comprising a housing in which the three-dimensional porous substrate is disposed.

22. (Amended) The flow-through device of Claim 21, in which said housing is selected from the group consisting of a syringe barrel, a pipette, a disposable pipette tip, a chromatography column, a spin column, a microchannel, a capillary and a multi-well plate.

23. (Amended) A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 1 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

26. (Thrice Amended) The method of Claim 23 or 64 in which said target nucleic acid is applied to the flow-through device under conditions wherein it hybridizes with said capture polynucleotide in less than one minute.

27. (Thrice Amended) The method of Claim 23 in which said porous substrate of said flow-through device has an average pore size of about 1 μm to about 250 μm.

28. (Thrice Amended) The method of Claim 64 in which the density or surface concentration of said capture polynucleotide is about 2×10^{-19} to 2×10^{-15} nmol/nm^2.

29. (Twice Amended) The method of Claim 23 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device.

30. (Twice Amended) The method of Claim 23 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device *via* a phosphodiester, phosphorothioate or phosphoramidate linkage.

31. (Twice Amended) The method of Claim 23 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device *via* a carboxyamide linkage.

32. (Thrice Amended) The method of Claim 23 or 64 in which said capture polynucleotide is covalently attached to the porous substrate of the flow-through device *via* a linker.

35. (Thrice Amended) The method of Claim 23 or 64 in which said porous substrate of said flow-through device has a void volume in the range of 0.1 μl/cm^2 to about 100 μl/cm^2.

36. (Thrice Amended) The method of Claim 23 or 64 which further includes the step of washing said hybridized complex.

40. (Thrice Amended) A method of determining whether a sample contains a target nucleic acid, said method comprising the steps of:

(a) flowing a sample suspected of containing a target nucleic acid through a flow-through device according to Claim 1 or 60 under conditions wherein the target nucleic acid and capture polynucleotide hybridize; and

(b) detecting the presence of hybrids, wherein a positive detection indicates the presence of the target nucleic acid in the sample.

41. The method of Claim 40, in which said target nucleic acid bears a reporter moiety and hybrids are detected by detecting the presence of said reporter moiety.

44. (Thrice Amended) A kit for capturing a target nucleic acid of interest from a sample, comprising:

a) a flow-through device according to Claim 1 or 60; and

b) a housing into which the flow-through device can be disposed.

50. (Four Times Amended) A kit for capturing a target nucleic acid from a sample comprising:

a) a flow-through device according to Claims 1 or 60; and

b) a capture polynucleotide capable of being covalently attached to the porous substrate.

51. The kit of Claim 50 further including a linker capable of being covalently attached to the porous substrate and the capture polynucleotide.

52. (Four Times Amended) A kit for capturing a target nucleic acid from a sample comprising:

a) a flow-through device according to Claims 1 or 60; and

b) means for generating a capture polynucleotide which is capable of hybridizing to the target nucleic acid and which is capable of being covalently attached to the porous substrate.

60. (Twice amended) A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 10 μm to about 100 μm and a porosity in the range of about 25 to 80% and having immobilized thereon a capture polynucleotide capable of hybridizing to the target nucleic acid.

64. A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 60 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

65. The kit of Claim 50 or 51 in which the porous substrate is activated with about 6×10^{-17} to 9×10^{-15} nmol/nm^2 of a reactive group.

72. A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of polyethylene, polystyrene, polycarbonate and polypropylene and having a porosity in the range of about 25 to 80% and having immobilized thereon a capture polynucleotide capable of hybridizing to the target nucleic acid.

73. A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of glass, polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 10 μm to about 100 μm and a porosity in the range of about 25 to 80% and having immobilized thereon about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid.

74. A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of glass, polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 10 μm to about 100 μm and a porosity in the range of about 25 to 80% and having immobilized thereon a capture polynucleotide capable of hybridizing to the target nucleic acid, wherein said porous substrate is about 1 mm to 20 mm thick.

75. A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of glass, polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 10 μm to about 100 μm and having immobilized thereon about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid, wherein said porous substrate is about 1 mm to 20 mm thick.

76. A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of glass, polyethylene, polystyrene, polycarbonate and polypropylene and having a porosity in the range of about 25 to 80% and having immobilized thereon about 6×10^{-17} to 6×10^{-16} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid, wherein said porous substrate is about 1 mm to 20 mm thick.

77. A flow-through device for capturing a target nucleic acid, comprising a three-dimensional porous substrate composed of a polymeric material selected from the group consisting of glass, polyethylene, polystyrene, polycarbonate and polypropylene and having an average pore size of about 1 μm to about 250 μm and a porosity in the range of about 25 to 80% and having immobilized thereon about 2×10^{-19} to 2×10^{-15} nmol/nm^2 of a capture polynucleotide which is capable of hybridizing to the target nucleic acid, wherein said porous substrate is about 1 mm to 20 mm thick.

78. (Amended) The flow-through device of Claim 72, 73, 74, 75, 76 or 77 in which said capture polynucleotide is covalently attached to the porous substrate.

79. (Amended) The flow-through device of Claim 72, 73, 74, 75, 76 or 77 in which said porous substrate has a void volume in the range of about 1 μl/cm^2 to about 100 μl/cm^2.

80. (Amended) The flow-through device of Claim 72, 73, 74, 75, 76 or 77 in which the capture polynucleotide is covalently immobilized on the porous substrate via its 5'- or 3'-terminal residue.

81. (Amended) The flow-through device according to Claim 72, 73, 74, 75, 76 or 77 further comprising a housing in which the three-dimensional porous substrate is disposed.

82. (Amended) A method of capturing a target nucleic acid from a sample, said method comprising flowing a sample containing or suspected of containing a target nucleic acid through a flow-through device according to Claim 72, 73, 74, 75, 76 or 77 under conditions wherein said target nucleic acid and capture polynucleotide hybridize to one another to form a hybridized complex, thereby capturing the target nucleic acid.

83. The method of Claim 82 in which said target nucleic acid is applied to the flow-through device under conditions wherein it hybridizes with said capture polynucleotide in less than one minute.